REMARKS

I. Status of the Claims

Claims 1-8 are withdrawn.

Claims 9, 11, are amended.

Claims 9-17 are pending.

II. Interview Summary

Applicant thanks Supervisor Padmanabhan and Examiner Claytor for the Interview of October 10, 2007 with applicant's representation Richard Lazarus and Alice Martin, and the inventor Joel Bernstein, M.D. Suggestions on claim amendments were made to move this case toward allowance. A question of total daily dosage as distinct from unit dose, e.g. dose per capsule, arose. Claim amendments with support from the specification were suggested, as long as the claim scope was not within the art, e.g. in Examples 1-46 in Caruso. Dr. Bernstein pointed out that if multiple doses are taught per day, the daily dose must be divided by the number of doses to arrive at the unit dose.

The references requested by the previous examiner in a previous Interview regarding low and standard doses were in Exhibits A and B of record.

III. The Inventor Had Possession of the Elements of Claims 13 and 16.

Claims 13 and 16 were rejected under 35 U.S.C. §112, first paragraph.

As discussed during the interview, there is a support for "unit doses of from about 25 mg to about 1mg" of non-narcotic analgesic, and "unit doses of 10 mg or less" of a tricyclic anti-depressant."

[00010], [00011]

Applicant agrees that in the specification [00010 and 00011] supports:

[00010] 0.5 gm-2.6 gm daily; 0.5-2 gm/day acetaminophen; 0.6-2.6 gm/day aspirin; 0.6-1.8 gm/day ibuprofen; and in [00011] 2.5 mg to 25 mg/day (5 mg to 20 mg, 10-15 mg/day) of a tricyclic antidepressant.

As Dr. Bernstein explained, these are **daily** doses. In contrast, unit doses are daily doses divided by the number of administrations of the unit doses. Claims 13 and 16 relate unit doses. The examples provide support for conversion of the daily doses in [0010 and 0011] to unit doses.

[00015] Example 1: 500 mg acetaminophen + 5 mg doxepin (unit dose).

[00016] Example 2: 5 mg doxepin + 650 mg aspirin, unit dose, twice daily.

[00017] Example 3: 10 mg doxepin + 600 mg ibuprofen.

In Example 1, the patient took a unit dose of 5mg doxepin and 500 mg acetaminophen. That supports claims 13 and 16 and is consistent with [0008] (25 mg/day or less) and [00010 and 00011] tricyclic antidepressant.

The unit dose in Example 2 is 5 mg doxepin and 650 mg. aspirin; the daily dose is 10 mg doxepin and 1300 mg aspirin (2 unit doses).

The unit dose in Example 3 is 10 mg doxepin and 600 mg ibuprofen.

All these doses are not only within the scope of claims 13 and 16, but fit the inventive combination of "low dose" tricyclic antidepressant, with a "standard dose" non-narcotic analgesic.

IV. Caruso Does Not Teach All Claim Elements Therefore Does Not Anticipate

Claims 9-15 and 17 were rejected over Caruso under 35 U.S.C. §102(b).

Caruso does not teach all claim elements, therefore does not anticipate claims 9-15 and 17.

Caruso relates administering an antidepressant "prior to, with or following the administration of a nontoxic NMDA receptor antagonist." (Abstract)

Caruso gives dextromethorphan as an example of a nontoxic substance that blocks an NMDA receptor binding site. The antidepressants include cyclic antidepressants.

For dosage levels, Caruso refers to the PDR (1996) and Goodman and Gilman's well known book. However, an example presented is "dosage of from about 50 to 360 mg/day" of the tricyclic antidepressant imipramine hydrochloride," combined with "from about 30 to about 120 mg/day of dextromethorphan." (page 5, lines 5-24).

The examiner refers to Caruso's Examples 1-46 to reject present claims; but these nontoxic NMDA receptor blockers of Caruso are not the class of drugs of non-narcotic analgesics claimed in the present application.

The non-narcotic analgesics as used in the pending application are distinguished by Caruso as shown in claims 8 and 11 of Caruso to "the other pharmacologically active substance," and as "active additional components" in some of the Examples 1-46.

Caruso does not teach a combination of cyclic antidepressants and non-narcotic analgesics; Caruso teaches a combination of antidepressants and a **nontoxic NMDA receptor antagonist**.

The examiner cites to page 7, lines 10-24 of Caruso for support for the rejection not clarifying that the NMDA receptor antagonist **must** be present. The present application does **not** teach a nontoxic NMDA receptor antagonist so it cannot be present in the pending claims.

The examiner is incorrect in interpreting the meaning of "consisting essentially of" as equivalent to "comprising." Case law has defined "consisting essentially of" as intermediate between "consisting of" and "comprising" "consisting essentially of" includes only materials specified in the claim "and those that do not materially affect the basic and novel characteristics of the claimed invention." Introducing the NSAD receptor antagonists required by Caruso, would not be consistent with the novelty and characteristics of the present invention which does **not** include dangerous drugs such as NSAD receptor antagonists [e.g. "consisting essentially of" - is defined as materials specified in the claims" and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. *In re Herz*, 537 F.2d 549, 551-52 (CCPA 1976) as cited in MPEP 2111.03; *Boeing Co. v. United States*, 80 U.S.P.Q. 2d (BNA) 1108 (2005); *Talbert Fuel Sys. Patents Co. v. Unocol Corp.*, 51 U.S.P.Q. 2d BNA 1363 (Fed. Cir. 2002).

No teaching from Caruso relates doses that can be compared to the present claims because the combinations of Caruso **require** nontoxic NMDA receptor blockers. No one of skill in the art would come away from reading Caruso motivated to combine just an antidepressant with an "additional," optional component that in some of Caruso's examples are non-narcotic analgesics. One of skill in the art would expect that an NMDA receptor blocker was **required** to achieve pain relief with an antidepressant. And if one of skill in the art **omitted** the required NMDA receptor blocker, there would be no expectation that using the additional component, which is an essential ingredient of the present claims, would be at the dose levels in Examples 1-46.

If a recipe called for eggs, milk and flour, and another only includes milk and flour, the result could hardly be equivalent.

V. A Prima Facie Case of Obviousness Is Not Established

Claims 9-11, 13-14 and 16-17 were rejected as obvious over Kakuyama.

Claims 12 and 15 were rejected as obvious over Kakuyama and Caruso.

Claim 16 was rejected as obvious over Caruso.

Claims 9-17 were rejected as obvious over Crawford and Lombardino.

The examiner bases an obviousness rejection of claims 9-11, 13-14 and 16-17 on Kakuyama.

A prima facie case of obviousness is not established because all elements of the claims are not taught by the publications cited. The examiner admits that Kakuyama "does not specifically teach that the 'standard dose' of naproxen and 'low dose' of amitriptyline are provided in the same composition." (Office Action, page 7).

However, contrary to the examiner's argument, nether does Kakuyama teach even administering a tricyclic depressant and a non-narcotic analgesic one after the other.

The examiner's citations to Kakuyama must be taken in context: Page 125, Rhand, 4th full paragraph recites studies of others, and reports controversy about the effects of amitriptyline, not the "desirability of providing a non-narcotic analgesic...." as the examiner states. (Office Action, page 7).

The examiner invokes obviousness if each single component "is taught by the prior art to be useful for the same purpose" but even if the components of the tricyclic depressants were taught in the prior art to alleviate pain, why would one of skill in the art give 2 drugs if each singly was expected to achieve the same result – pain relief?

The examiner also admits that:

> Kakuyama et al. does not specifically teach providing the amitriptyline in the form of one of the acid addition salts as recited in claim 12. Kakuyama et al. also does not specially teach the pharmaceutically acceptable vehicles such as tablets, capsules, caplets, etc. as recited in claim 15.

Office Action pages 9-10

Caruso is invoked to substitute for the omissions of Kakuyama , but deficiencies in Caruso were discussed in the previous section herein.

Crawford and Lombardino are combined by the examiner to reject claims 9-17 as obvious.

As the examiner admits, Crawford, like Caruso, teaches "a non-steroidal anti-inflammatory drug" with an antidepressant. Crawford only teaches piroxicam. The present claims do **not** include

"a non-steroidal anti-inflammatory drug." The present claims **do** include a non-narcotic analgesic. Crawford does not teach a combination of non-narcotic analgesics and anti-depressants. Therefore doses in Crawford cannot be extrapolated to the present claims even if the examiner is trying to equate non-steroid anti-inflammatory drugs with non-narcotic analgesics.

As the examiner admits, Lombardino only teaches an anti-inflammatory.

On pages 13-15 the examiner continues to argue that it would be obvious to combine Crawford and Lombardino to provide

> a suitable anti-inflammatory composition for the treatment of gastric irritation.

There is no prima facie case because, regardless of which publications are combined, they do not cover the 2 claimed ingredients. Nor can doses of one class of drugs be extrapolated to another.

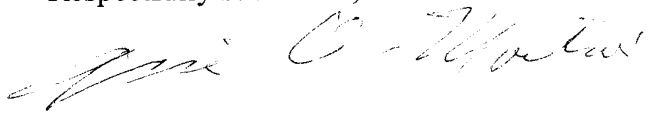
"To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references." MPEP § 706.02(j) *quoting Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). A determination of obviousness requires that "the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved." *KSR International Co. v. Teleflex, Inc.*, -- U.S. --, 127 S.Ct. 1727, 1734, 82 U.S.P.Q.2d 1385 (2007) *quoting Graham v. John Deer Co.*, 383 U.S. 1, 17 (1966). In making a determination of obviousness by looking at the teachings of multiple patents, one should consider

> the effects of demands known to the design community or present in the market place; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. <u>To facilitate review, this analysis should be made explicit.</u>

KSR, 127 S.Ct. at 1740-41 (*emphasis added*). "[A] patent composed of several elements is not proved obvious merely by demonstrating the each of its elements was, indepe6ndently, known in the prior art." *Id.* at 1741.

No other fees are believed due at this time, however, please charge any additional deficiencies or credit any overpayments to deposit account number 12-0913 with reference to our attorney docket number (41957-102748).

Respectfully submitted,



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